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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/598,709	06/08/2007	Koichi Shudo	P28752	9187

7055 7590 05/13/2010

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EXAMINER	
RAMACHANDRAN, UMAMAHESWARI	
ART UNIT	PAPER NUMBER
1627	

NOTIFICATION DATE	DELIVERY MODE
05/13/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

gbpatent@gbpatent.com
pto@gbpatent.com

Office Action Summary	Application No.	Applicant(s)	
	10/598,709	SHUDO ET AL.	
	Examiner	Art Unit	
	UMAMAHESWARI RAMACHANDRAN	1627	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 March 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2, 5-19* is/are pending in the application.

4a) Of the above claim(s) *1 and 10-13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,5-9 and 14-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/26/2009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's election of species 4-[(5,6,7,8-tetrahydro-5,5,8,8-tetramethyl-2-naphthalenyl)carbamoyl]benzoic acid in the response dated 3/8/2010 is acknowledged. Applicants have elected the species with traverse and have argued that the office has not established why unity of invention was lacking. Applicants' have amended and added claims that include method claims in addition to the existing composition claims. The amendments necessitated to restrict the claims to the following groups.

1) Claim 1 - medicament (composition) comprising an active ingredient, a non natural retinoid

2) Claim 6 - A method of treating a neurodegenerative disease comprising administering 4-[(5,6,7,8-tetrahydro-5,5,8,8-tetramethyl-2-naphthalenyl)carbamoyl]benzoic acid or 4-[(3,5-bis-trimethylsilylphenyl) carboxamido]benzoic acid.

3) Claims 2, 5, 7-19 – A method of promoting memory consolidation comprising administering to a mammal a composition comprising a non natural retinoid.

The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons:

The technical feature shared by the above-listed species is retinoid 4-[(5,6,7,8-tetrahydro-5,5,8,8-tetramethyl-2-naphthalenyl)carbamoyl] benzoic acid and it is known in the prior art (Qing et al, J of Fluorine Chemistry, 96, 1999, 159-61). This was discussed with Atty. Arnold Turk in an interview (Apr 14 2010) and the Applicants' have

elected Group III, a method for promoting memory consolidation and the species 4-[(5,6,7,8-tetrahydro-5,5,8,8-tetramethyl-2-naphthalenyl)carbamoyl]benzoic acid for examination purposes. To address Applicants' arguments, as cited above, the non natural retinoid, 4-[(5,6,7,8-tetrahydro-5,5,8,8-tetramethyl-2-naphthalenyl)carbamoyl] benzoic acid is known in the art and the groups lack the special technical feature. Accordingly, the restriction election is made Final.

Claims 2, 5, 7- 9, 13-16, 18, 19 read on the elected species. Claims 1, 2, 5-19 are pending, claims 3-4 have been cancelled and claims 1, 6, 10-12, 17 are withdrawn from consideration. Claims 2, 5, 7- 9, 13-16, 18, 19 are examined on the merits herein.

Application Priority

This application is a national stage entry of PCT/JP05/04051, International Filing Date: 03/09/2005, PCT/JP05/04051 and Claims Priority from Provisional Application 60622618, filed 10/28/2004, claims foreign priority to 2004-066996 , filed 03/10/2004.

Information Disclosure Statement

The information disclosure statement (IDS) filed on 5/26/2009 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the IDS is being considered by the Examiner.

.Specification

The disclosure is objected to because of the following informalities: Table 2, of the specification has listed Am8 as the drug administered but it should be Am80. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2, 5, 7- 9, 13-16, 18, 19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is not clear from the limitation of claim 7 that administering a prophylactically effective amount of the composition will promote memory consolidation or prevent memory consolidation because the term 'prophylactic' is defined as a treatment designed and used to prevent a disease from occurring. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

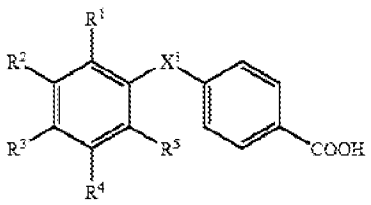
> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2, 5, 7- 9, 13-16, 18, 19 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The specification does not provide enablement for prophylactic treatment of dysfunction of promoting memory consolidation comprising administering 4-[(5,6,7,8-tetrahydro-5,5,8,8-tetramethyl-2-naphthalenyl)carbamoyl] benzoic acid.

Attention is directed to *In re Wands,* 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman,* 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and, (8) the quantity of experimentation necessary.

(1, 5) The nature of the invention and the Breadth of the Claims:

The instant claims are drawn to a method of prophylactic and/or therapeutic treatment for promoting memory consolidation comprising administering a non natural retinoid having a basic skeleton comprising an aromatic ring bound with an aromatic carboxylic acid or tropolone bound by a bridging group. The claims are very broad with respect to the non natural retinoids having a basic skeleton comprising an aromatic ring bound with an aromatic carboxylic acid or tropolone bound by a bridging group. The compounds claimed with a basic skeleton comprising an aromatic ring bound with an aromatic carboxylic acid can encompass aryl, heteroaryl, heteroarylalkyl etc and the review of the specification teaches compounds of formula I



and few compounds that include 4-[(5,6,7,8-tetrahydro-5,5,8,8-tetramethyl-2-naphthalenyl)carbamoyl]benzoic acid or 4-[(3,5-bis-trimethylsilylphenyl)carboxamido] benzoic acid, dibenzo[b,f][1,4]thiazepinylbenzoic acid, 4-[2,3-(2,5-dimethyl-2,5-hexano)dibenzo[b,f][1,4]-thiazepin-11-yl]benzoic acid, 4-[5-(4,7-dimethylbenzofuran-2-yl)pyrrol-2-yl]benzoic acid. The scope of the claims is very large with respect to the number of compounds that can be used in promoting memory consolidation. The term 'prophylactic' is defined as a treatment designed and used to prevent a disease from occurring.

(***2) The state of the prior art:***

The prior art Teng et al. (U.S. 5,965,606) teaches retinoid compounds which act specifically or selectively on RAR receptor subtypes and further teaches that the retinoid compounds are useful in treating neurodegenerative conditions like Alzheimer's disease (See Abstract, col. 1, lines 55-56). Yamakawa et al. (Applicant cited IDS: J Med Chem 1990, 33, 1430-37) teaches retinoidal compounds having a basic skeleton comprising an aromatic ring bound with an aromatic carboxylic acid (p 1431). Goodman (Applicant cited IDS: PNAS, 2003, 100, 5, 2901-05) teaches that the late onset Alzheimer's disease is influenced by the availability in brain of retinoic acid. Hashimoto (Cell Structure and Function, 16, 113-123, 1991) teaches the compound Am-80 (elected species claimed) as a retinobenzoic acid (p 114). Furthermore the reference teaches that Am80 binds to various RAR receptors (Table 1). The reference in Fig. 4 teaches various retinobenzoic acid compounds with various activities towards the receptors and with different inhibition constants. Etchamendy (Applicant cited IDS: J Neurosci, 2001,

Aug 21(16) p 6423-29) teaches that Vitamin A and its derivatives, the retinoids have been implicated recently in the synaptic plasticity of the hippocampus and might therefore play a role in associated cognitive functions.

(3) The relative skill of those in the art:

The relative skill of those in the pharmaceutical development and medical treatment arts is high, requiring advanced education and training.

(4) The predictability of the art:

Applicants have claimed compounds of retinoids having a basic skeleton comprising an aromatic ring bound with an aromatic carboxylic acid or tropolone bound by a bridging ring. Though prior art teaches some compounds and the specification has cited few compounds and have made use of few such compounds in a method of promoting memory consolidation, the claims encompass a large number of compounds including aryl, heteroaryl, heteroalkylaryl compounds for an aromatic ring structure bound to carboxylic acid it is not predicable from what is known to synthesize all the compounds claimed. It is noted that the execution of chemical reactions is dependent upon numerous variable factors that are essential for producing the intended compound, such as, but not limited to, the starting materials to be employed, the temperature at which the reaction(s) should be carried out, solvents, reaction catalysts, molar quantities, surface area, pressure, activation energies, etc. In view of such a number of factors, and further in view of the high degree of variability for each single factor that must be taken into account in order to provide an accurate means for producing the claimed compounds of formula (I), the state of the art with regard to

chemical reactions in general is highly complex and sufficiently unpredictable such that the skilled artisan would have been required to undertake undue experimentation to determine the exact conditions and manner and/or process of execution to arrive at those conditions that would have been amenable to actually producing the compound of formula (I) as claimed in the absence of detailed guidance to this effect. It is not predictable from the prior art or from the specification that the dysfunction of memory consolidation can be completely prevented.

(6, 7) The amount of guidance given and the presence of working examples:

The specification provides guidance to a method of promoting memory consolidation comprising administering compounds including Am80, Tac10, HX63 in rats. The specification fails to provide any guidance to what concentrations of non natural retinoids having a basic skeleton comprising an aromatic ring bound with an aromatic carboxylic acid or tropolone bound by a bridging group will be prophylactically effective in promoting memory consolidation. Also, the specification does not provide guidance to what bridging groups are bound to a tropolone. The specification does not provide any guidance towards the prevention of dysfunction of memory consolidation.

(8) The quantity of experimentation necessary:

Given that the instant claims encompass complete prophylactic treatment (prevention) of the dysfunction of memory consolidation, Applicants have not provided any guidance to completely prevent the dysfunction. Applicant fails to provide information sufficient to practice the claimed invention, absent undue experimentation.

The burden of enabling the prevention of dysfunction of memory consolidation would be much greater than that of enabling the treatment of such condition. In the instant case, the specification does not provide guidance as to how one skilled in the art would accomplish the objective of preventing such conditions or how a patient could be kept from every being susceptible to these conditions. Nor is there any guidance provided as to a specific protocol to be utilized in order to show the efficacy of the presently claimed active ingredients for preventing the above conditions. In addition, it will be an undue experimentation to one of ordinary skill in the art to synthesize all the compounds claimed, test them for the retinoidal activity and conduct experiments using the compounds in preventing the dysfunction of memory consolidation. Genetech, 108 F.3d at 1366 states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable."

Accordingly the claims are evaluated as a method for treating the dysfunction of memory consolidation and not as a method for preventing the dysfunction of memory consolidation comprising administering a non natural retinoid compound having a basic skeleton comprising an aromatic ring bound with an aromatic carboxylic acid or tropolone bound by a bridging group.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

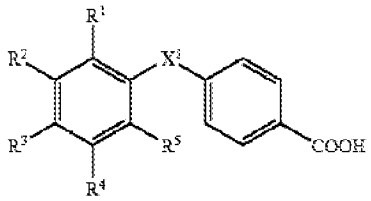
pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2, 5, 7- 9, 13-16, 18, 19 are rejected under 35 U.S.C. 112, first paragraph, because the specification and prior art while enabling for some compounds of non natural retinoids having a basic skeleton comprising an aromatic ring bound with an aromatic carboxylic acid or tropolone bound by a bridging group does not reasonably provide enablement for the compounds encompassed by the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. Specification provides no guidance as to what other bridging groups might be suitable to link to tropolone and there is no basis in the prior art directed to similar compounds having the same activity as herein. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Attention is directed to *In re Wands,* 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman,* 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and, (8) the quantity of experimentation necessary.

(1, 5) The nature of the invention and the Breadth of the Claims:

The instant claims are drawn to a method for promoting memory consolidation, comprising administering to a mammal in need thereof a prophylactically and/or therapeutically effective amount of a composition to promote memory consolidation comprising administering an active ingredient, a non-natural retinoid. The claims are very broad with respect to the non natural retinoids having a basic skeleton comprising an aromatic ring bound with an aromatic carboxylic acid or tropolone bound by a bridging group. The compounds claimed with a basic skeleton comprising an aromatic ring bound with an aromatic carboxylic acid can encompass aryl, heteroaryl, heteroarylalkyl etc and the review of the specification teaches compounds of formula I



and few compounds that include 4-[(5,6,7,8-tetrahydro-5,5,8,8-tetramethyl-2-naphthalenyl)carbamoyl]benzoic acid or 4-[(3,5-bis-trimethylsilylphenyl)carboxamido] benzoic acid, dibenzo[b,f][1,4]thiazepinylbenzoic acid, 4-[2,3-(2,5-dimethyl-2,5-hexano)dibenzo[b,f][1,4]-thiazepin-11-yl]benzoic acid, 4-[5-(4,7-dimethylbenzofuran-2-yl)pyrrol-2-yl]benzoic acid. The scope of the claims is very large with respect to the number of compounds that can be used in promoting memory consolidation.

(***2) The state of the prior art:***

The prior art Teng et al. (Applicant cited IDS: U.S. 5,965,606) teaches retinoid compounds which act specifically or selectively on RAR receptor subtypes and further

teaches that the retinoid compounds are useful in treating neurodegenerative conditions like Alzheimer's disease (See Abstract, col. 1, lines 55-56). Yamakawa et al. (Applicant cited IDS: J Med Chem 1990, 33, 1430-37) teaches retinoidal compounds having a basic skeleton comprising an aromatic ring bound with an aromatic carboxylic acid (p 1431). Goodman (Applicant cited IDS: PNAS, 2003, 100, 5, 2901-05) teaches that the late onset Alzheimer's disease is influenced by the availability in brain of retinoic acid. Hashimoto (Cell Structure and Function, 16, 113-123, 1991) teaches the compound Am-80 (elected species claimed) as a retinobenzoic acid (p 114). Furthermore the reference teaches that Am80 binds to various RAR receptors (Table 1). The reference in Fig. 4 teaches various retinobenzoic acid compounds with various activities towards the receptors and with different inhibition constants. Etchamendy (Applicant cited IDS: J Neurosci, 2001, Aug 21(16) p 6423-29) teaches that Vitamin A and its derivatives, the retinoids have been implicated recently in the synaptic plasticity of the hippocampus and might therefore play a role in associated cognitive functions.

(3) The relative skill of those in the art:

The relative skill of those in the pharmaceutical development and medical treatment arts is high, requiring advanced education and training.

(4) The predictability of the art:

Applicants have claimed compounds of retinoids having a basic skeleton comprising an aromatic ring bound with an aromatic carboxylic acid or tropolone bound by a bridging ring. Though prior art teaches some compounds and the specification has cited few compounds and have made use of few such compounds in a method of

promoting memory consolidation, the claims encompass a large number of compounds including aryl, heteroaryl, heteroalkylaryl compounds for an aromatic ring structure bound to carboxylic acid it is not predicable from what is known to synthesize all the compounds claimed. It is noted that the execution of chemical reactions is dependent upon numerous variable factors that are essential for producing the intended compound, such as, but not limited to, the starting materials to be employed, the temperature at which the reaction(s) should be carried out, solvents, reaction catalysts, molar quantities, surface area, pressure, activation energies, etc. In view of such a number of factors, and further in view of the high degree of variability for each single factor that must be taken into account in order to provide an accurate means for producing the claimed compounds of formula (I), the state of the art with regard to chemical reactions in general is highly complex and sufficiently unpredictable such that the skilled artisan would have been required to undertake undue experimentation to determine the exact conditions and manner and/or process of execution to arrive at those conditions that would have been amenable to actually producing the compound of formula (I) as claimed in the absence of detailed guidance to this effect.

(6, 7) The amount of guidance given and the presence of working examples:

The specification provides guidance to a method of promoting memory consolidation comprising administering compounds including Am80, Tac10, HX63 in rats. The specification fails to provide any guidance to what concentrations of non natural retinoids having a basic skeleton comprising an aromatic ring bound with an

aromatic carboxylic acid or tropolone bound by a bridging group will be prophylactically effective in promoting memory consolidation. Also, the specification does not provide guidance to what bridging groups are bound to a tropolone.

(8) The quantity of experimentation necessary:

In order to enable the instantly claimed methods that commensurate with the entire scope, a large quantity of experimentation would be necessary. With Applicants' guidance provided in the specification and what is known in the prior art the person of ordinary skill in the art would have to conduct experiments first design the non natural retinoids having a basic skeleton comprising an aromatic ring bound with an aromatic carboxylic acid or tropolone bound by a bridging group, then synthesize the compounds. test for its activity and then use those compounds in a method of promoting memory consolidation. It would be unduly burdensome to one of ordinary skill in the art, to search for ways to synthesize this embodiment of the claimed invention suitable for use in practicing the claimed composition, particularly since the skilled artisan is faced with such a breadth and variety of possible starting materials and reaction schema from which to choose. Applicant has (1) failed to provide any general information to which bridging groups be attached to tropolone and the synthetic procedures (2) failed to provide any working or prophetic examples directed to a possible method and/or manner of synthesis for those compounds. Furthermore a person of ordinary skill in the art has to conduct experiments to find the right dosage amounts for prophylactically effective or therapeutically effective concentration to use the compounds in a method of promoting memory consolidation. In order to practice the above claimed invention, one

of ordinary skill in the art would have to first envision formulation, dosage, duration, route and an appropriate animal model system to test the composition in a method of method of promoting memory consolidation. If unsuccessful, one of ordinary skill in the art would have to envision a modification in the formulation, dosage, duration, route of administration etc. and appropriate animal model system, or envision an entirely new combination of the above and test the system again. Therefore, it would require undue, unpredictable experimentation to practice the claimed invention of a method of promoting a memory consolidation comprising administering a prophylactically and/or therapeutically effective amount of non natural retinoids having a basic skeleton comprising an aromatic ring bound with an aromatic carboxylic acid or tropolone bound by a bridging group. Genetech, 108 F.3d at 1366 states that “a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion” and “patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable”.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2, 5, 7- 9, 13-16, 18, 19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 7 has a limitation 'wherein the non-natural retinoid comprises retinoid’, claim 14 has a limitation ‘wherein the retinoid comprises at least one’, claim 13 has a limitation 'wherein the retinoid

comprises' etc. It is not clear that the non natural retinoid is the retinoid having a basic skeleton comprising an aromatic ring bound with an aromatic carboxylic acid or tropolone bound by a bridging group or the non natural retinoid comprises another retinoid with specific structural features claimed. Appropriate correction is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

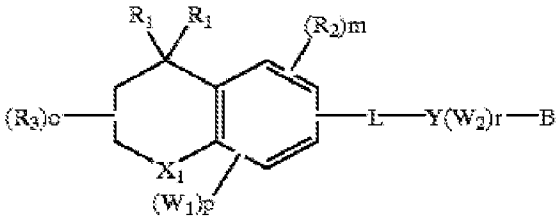
The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 2, 5, 7- 9, 13-16, 18, 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Teng et al. (Applicant cited IDS: U.S. 5,965,606) and Goodman (Applicant cited IDS: PNAS, 2003, 100, 5, 2901-05) and Etchamendy (Applicant cited IDS: J Neurosci, 2001, Aug 21(16) p 6423-29).

The prior art Teng et al. teaches retinoid compounds which act specifically or selectively on RAR receptor subtypes and further teaches that the retinoid compounds are useful in treating neurodegenerative conditions like Alzheimer's disease,

Parkinson's disease and stroke (See Abstract, col. 1, lines 55-56). The reference states that retinoids are useful for treating animals of the mammalian species including humans. Teng et al. teaches the compounds of formula I:



When X1=[C(R1)2]n, when R1=CH3, n=1, then X1= $-C(CH_3)_2$

R1=CH3

R3= no substituent, o=0

W1=no substituent when p = 0

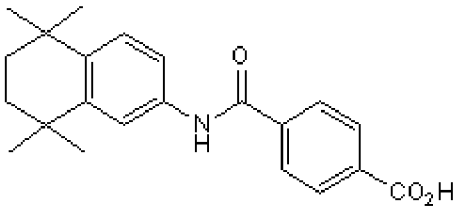
R2= no substituent when m=0

L= -NH-(CO)- when z=O

Y=phenyl

W2= no substituent when r=0

B=-COOH, then the prior art teaches the following compound



(AM80, elected species).

The reference teaches the compounds as retinoid compounds.

Goodman teaches that the late onset Alzheimer's disease is influenced by the availability in brain of retinoic acid (see abstract). It is known in the art that memory fixation disorders are main symptoms of Alzheimer's disease.

Etchamendy teaches that Vitamin A and its derivatives, the retinoids have been implicated recently in the synaptic plasticity of the hippocampus and might therefore play a role in associated cognitive functions (see abstract).

It would have been obvious to one having ordinary skill in the art at the time of the invention to have used a non-natural retinoid in a therapeutically effective amount to promote memory consolidation because of the prior art teachings. Teng et al. teaches compounds with an aromatic ring bound with an aromatic carboxylic acid including the elected species claimed as retinoid compounds. The reference further states that the retinoid compounds are useful in treating neurodegenerative diseases like Alzheimer's disease, Parkinson's disease etc. The teachings of Goodman and Etchamendy teach that retinoids can be useful in Alzheimer's disease and in improvement of cognitive functions. A person of ordinary skill in the art would have found it obvious to try a non natural retinoid compound such as 4-[(5,6,7,8-tetrahydro-5,5,8,8-tetramethyl-2-naphthalenyl)carbamoyl]benzoic acid (Am80) in promoting memory consolidation because, the compound is known in the art, easily available and known as a retinoid. A person of ordinary skill in the art would have been motivated to use Am80 in Alzheimer's patients to improve the memory impairment. Alzheimer's disease is an irreversible, progressive brain disease that slowly destroys memory and thinking skills and memory impairment is associated with Parkinson's disease. A person of ordinary skill in the art

would have elected to use the compounds of Teng et al, non natural retinoids in memory consolidation associated with Alzheimer's or Parkinson's disease because memory deficit and memory impairment is associated with both the diseases.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to UMAMAHESWARI RAMACHANDRAN whose telephone number is (571)272-9926. The examiner can normally be reached on M-F 8:30 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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